SEQUENCE LISTING

<110> Aranya Manosroi
Jiradej Manosroi
Chatchai Tayapiwatana
Friedrich Goetz
Rolf-Guenther Werner

<120> Methods for Large Scale Production of Recombinant DNA-Derived tPA or K2S Molecules

<130> 0652.2190001

<150> 60/268,574
<151> 2001-02-15

<150> GB 0027779.8
<151> 2000-11-14

<160> 25

<170> PatentIn Ver. 2.1

<210> 1
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: coding sequence of N-terminal part of K2S protein

<400> 1
tctgagggaa acagtgac 18

<210> 2
<211> 1128
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: coding sequence for OmpA-K2S fusion protein

<400> 2
atgaaaaaga cagctatcgc gattgcagtg gcactggctg gtttcgctac cgtggcccag 60
gcggcctctg agggaaacag tgactgctac tttgggaatg ggtcagccta ccgtggcacg 120
cacagcctca ccgagtcggg tgcctcctgc ctcccgtgga attccatgat cctgataggc 180
aaggtttaca cagcacagaa ccccagtgcc caggcactgg gcctgggcaa acataattac 240
tgccggaatc ctgatgggga tgccaagccc tggtgccacg tgctgaagaa ccgcaggctg 300
acgtgggagt actgtgatgt gccctcctgc tccacctgcg gcctgagaca gtacagccag 360
cctcagtttc gcatcaaagg agggctcttc gccgacatcg cctcccaccc ctggcaggct 420
gccatctttg ccaagcacag gaggtcgccc ggagagcggt tcctgtgcgg gggcatactc 480
atcagctcct gctggattct ctctgccgcc cactgcttcc aggagaggtt tccgccccac 540
cacctgacgg tgatcttggg cagaacatac cgggtggtcc ctggcgagga ggagcagaaa 600
tttgaagtcg aaaaatacat tgtccataag gaattcgatg atgacactta cgacaatgac 660
attgcgctgc tgcagctgaa atcggattcg tcccgctgtg cccaggagag cagcgtggtc 720
cgcactgtgt gccttccccc ggcggacctg cagctgccgg actggacgga gtgtgagctc 780
tccggctacg gcaagcatga ggccttgtct cctttctatt cggagcggct gaaggaggct 840
catgtcagac tgtacccatc cagccgctgc acatcacaac atttacttaa cagaacagtc 900

accgacaaca tgctgtgtgc tggagacact cggagcggcg ggccccaggc aaacttgcac 960
gacgcctgcc agggcgattc gggaggcccc ctggtgtgtc tgaacgatgg ccgcatgact 1020
ttggtgggca tcatcagctg gggcctgggc tgtggacaga aggatgtccc gggtgtgtac 1080
acaaaggtta ccaactacct agactggatt cgtgacaaca tgcgaccg 1128

<210> 3
<211> 66
<212> DNA
<213> Escherichia coli

<400> 3
atgaaaaaga cagctatcgc gattgcagtg gcactggctg gtttcgctac cgtggcccag 60
gcggcc 66

<210> 4
<211> 1065
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: coding sequence for K2S protein

<400> 4
tctgagggaa acagtgactg ctactttggg aatgggtcag cctaccgtgg cacgcacagc 60
ctcaccgagt cgggtgcctc ctgcctcccg tggaattcca tgatcctgat aggcaaggtt 120
tacacagcac agaaccccag tgcccaggca ctgggcctgg gcaaacataa ttactgccgg 180
aatcctgatg gggatgccaa gccctggtgc cacgtgctga agaaccgcag gctgacgtgg 240
gagtactgtg atgtgccctc ctgctccacc tgcggcctga gacagtacag ccagcctcag 300
tttcgcatca aaggagggct cttcgccgac atcgcctccc acccctggca ggctgccatc 360
tttgccaagc acaggaggtc gcccggagag cggttcctgt gcgggggcat actcatcagc 420
tcctgctgga ttctctctgc cgcccactgc ttccaggaga ggtttccgcc ccaccacctg 480
acggtgatct tgggcagaac ataccgggtg gtccctggcg aggaggagca gaaatttgaa 540
gtcgaaaaat acattgtcca taaggaattc gatgatgaca cttacgacaa tgacattgcg 600
ctgctgcagc tgaaatcgga ttcgtcccgc tgtgcccagg agagcagcgt ggtccgcact 660
gtgtgccttc ccccggcgga cctgcagctg ccggactgga cggagtgtga gctctccggc 720
tacggcaagc atgaggcctt gtctcctttc tattcggagc ggctgaagga ggctcatgtc 780
agactgtacc catccagccg ctgcacatca caacatttac ttaacagaac agtcaccgac 840
aacatgctgt gtgctggaga cactcggagc ggcgggcccc aggcaaactt gcacgacgcc 900
tgccagggcg attcgggagg ccccctggtg tgtctgaacg atggccgcat gactttggtg 960
ggcatcatca gctggggcct gggctgtgga cagaaggatg tcccgggtgt gtacacaaag 1020
gttaccaact acctagactg gattcgtgac aacatgcgac cgtga 1065

<210> 5
<211> 1128
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: coding sequence for OmpA-K2S fusion protein

<400> 5
atgaaaaaga cagctatcgc gattgcagtg gcactggctg gtttcgctac cgtggcccag 60
gcggcctctg agggaaacag tgactgctac tttgggaatg ggtcagccta ccgtggcacg 120
cacagcctca ccgagtcggg tgcctcctgc ctcccgtgga attccatgat cctgataggc 180
aaggtttaca cagcacagaa ccccagtgcc caggcactgg gcctgggcaa acataattac 240
tgccggaatc ctgatgggga tgccaagccc tggtgccacg tgctgaagaa ccgcaggctg 300
acgtgggagt actgtgatgt gccctcctgc tccacctgcg gcctgagaca gtacagccag 360

cctcagtttc gcatcaaagg agggctcttc gccgacatcg cctcccaccc ctggcaggct 420
gccatctttg ccaagcacag gaggtcgccc ggagagcggt tcctgtgcgg gggcatactc 480
atcagctcct gctggattct ctctgccgcc cactgcttcc aggagaggtt tccgccccac 540
cacctgacgg tgatcttggg cagaacatac cgggtggtcc ctggcgagga ggagcagaaa 600
tttgaagtcg aaaaatacat tgtccataag gaattcgatg atgacactta cgacaatgac 660
attgcgctgc tgcagctgaa atcggattcg tcccgctgtg cccaggagag cagcgtggtc 720
cgcactgtgt gccttccccc ggcggacctg cagctgccgg actggacgga gtgtgagctc 780
tccggctacg gcaagcatga ggccttgtct cctttctatt cggagcggct gaaggaggct 840
catgtcagac tgtacccatc cagccgctgc acatcacaac atttacttaa cagaacagtc 900
accgacaaca tgctgtgtgc tggagacact cggagcggcg ggccccaggc aaacttgcac 960
gacgcctgcc agggcgattc gggaggcccc ctggtgtgtc tgaacgatgg ccgcatgact 1020
ttggtgggca tcatcagctg gggcctgggc tgtggacaga aggatgtccc gggtgtgtac 1080
acaaaggtta ccaactacct agactggatt cgtgacaaca tgcgaccg 1128

<210> 6
<211> 66
<212> DNA
<213> Escherichia coli

<400> 6
atgaaaaaga cagctatcgc gattgcagtg gcactggctg gtttcgctac cgtggcccag 60
gcggcc 66

<210> 7
<211> 1065
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: coding
sequence for K2S protein

<400> 7
tctgagggaa acagtgactg ctactttggg aatgggtcag cctaccgtgg cacgcacagc 60
ctcaccgagt cgggtgcctc ctgcctcccg tggaattcca tgatcctgat aggcaaggtt 120
tacacagcac agaaccccag tgcccaggca ctgggcctgg gcaaacataa ttactgccgg 180
aatcctgatg gggatgccaa gccctggtgc cacgtgctga agaaccgcag gctgacgtgg 240
gagtactgtg atgtgccctc ctgctccacc tgcggcctga gacagtacag ccagcctcag 300
tttcgcatca aaggagggct cttcgccgac atcgcctccc acccctggca ggctgccatc 360
tttgccaagc acaggaggtc gcccggagag cggttcctgt gcgggggcat actcatcagc 420
tcctgctgga ttctctctgc cgcccactgc ttccaggaga ggtttccgcc ccaccacctg 480
acggtgatct tgggcagaac ataccgggtg gtccctggcg aggaggagca gaaatttgaa 540
gtcgaaaaat acattgtcca taaggaattc gatgatgaca cttacgacaa tgacattgcg 600
ctgctgcagc tgaaatcgga ttcgtcccgc tgtgcccagg agagcagcgt ggtccgcact 660
gtgtgccttc ccccggcgga cctgcagctg ccggactgga cggagtgtga gctctccggc 720
tacggcaagc atgaggcctt gtctcctttc tattcggagc ggctgaagga ggctcatgtc 780
agactgtacc catccagccg ctgcacatca caacatttac ttaacagaac agtcaccgac 840
aacatgctgt gtgctggaga cactcggagc ggcgggcccc aggcaaactt gcacgacgcc 900
tgccagggcg attcgggagg ccccctggtg tgtctgaacg atggccgcat gactttggtg 960
ggcatcatca gctggggcct gggctgtgga cagaaggatg tcccgggtgt gtacacaaag 1020
gttaccaact acctagactg gattcgtgac aacatgcgac cgtga 1065

<210> 8
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: OmpA-K2S

fusion protein

<400> 8

```
Met Lys Lys Thr Ala Ile Ala Ile Ala Val Ala Leu Ala Gly Phe Ala
 1               5                  10                  15

Thr Val Ala Gln Ala Ala Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly
            20                  25                  30

Asn Gly Ser Ala Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala
        35                  40                  45

Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr
    50                  55                  60

Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr
65                  70                  75                  80

Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys
                85                  90                  95

Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr
            100                 105                 110

Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly
        115                 120                 125

Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala
    130                 135                 140

Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu
145                 150                 155                 160

Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg
                165                 170                 175

Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val
            180                 185                 190

Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val
        195                 200                 205

His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu
    210                 215                 220

Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val
225                 230                 235                 240

Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr
                245                 250                 255

Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe
            260                 265                 270

Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser
        275                 280                 285

Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met
    290                 295                 300

Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His
305                 310                 315                 320
```

```
Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp
                325                 330                 335

Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly
            340                 345                 350

Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp
        355                 360                 365

Trp Ile Arg Asp Asn Met Arg Pro Gly
    370                 375
```

<210> 9
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: peptide sequence

<400> 9
Ser Glu Gly Asn
1

<210> 10
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: peptide sequence

<400> 10
Ser Glu Gly Asn Ser Asp
1   5

<210> 11
<211> 354
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 174-527

<400> 11

```
Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg
  1               5                  10                  15

Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn
            20                  25                  30

Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala
        35                  40                  45

Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly
    50                  55                  60
```

```
Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp
 65                  70                  75                  80

Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr
                85                  90                  95

Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala
            100                 105                 110

Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro
        115                 120                 125

Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile
    130                 135                 140

Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu
145                 150                 155                 160

Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu
                165                 170                 175

Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp
            180                 185                 190

Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser
        195                 200                 205

Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro
    210                 215                 220

Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly
225                 230                 235                 240

Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys
                245                 250                 255

Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His
            260                 265                 270

Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr
        275                 280                 285

Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp
    290                 295                 300

Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val
305                 310                 315                 320

Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly
                325                 330                 335

Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met
            340                 345                 350

Arg Pro
```

<210> 12
<211> 331
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 197-527

<400> 12

```
Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys
  1               5                  10                  15

Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys
             20                  25                  30

His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His
         35                  40                  45

Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser
     50                  55                  60

Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile
 65                  70                  75                  80

Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala
                 85                  90                  95

Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly
            100                 105                 110

Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe
        115                 120                 125

Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr
    130                 135                 140

Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys
145                 150                 155                 160

Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile
                165                 170                 175

Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser
            180                 185                 190

Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro
        195                 200                 205

Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu
    210                 215                 220

Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr
225                 230                 235                 240

Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr
                245                 250                 255

Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala
            260                 265                 270

Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
        275                 280                 285

Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu
    290                 295                 300

Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn
```

305 310 315 320

Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
325 330

<210> 13
<211> 339
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 193-527, modified

<400> 13
Ser Glu Gly Asn Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp
1 5 10 15

Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser
20 25 30

Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp
35 40 45

Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr
50 55 60

Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln
65 70 75 80

Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile
85 90 95

Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser
100 105 110

Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp
115 120 125

Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His
130 135 140

Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu
145 150 155 160

Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp
165 170 175

Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp
180 185 190

Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu
195 200 205

Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser
210 215 220

Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu
225 230 235 240

Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln

245 250 255

His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp
260 265 270

Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly
275 280 285

Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu
290 295 300

Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro
305 310 315 320

Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn
325 330 335

Met Arg Pro

<210> 14
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 193-527, modified

<400> 14
Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
1 5 10 15

Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
20 25 30

Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
35 40 45

Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
50 55 60

Asp Val Pro Ser Ser Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
65 70 75 80

Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
85 90 95

Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
100 105 110

Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
115 120 125

Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
130 135 140

Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
145 150 155 160

Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr

```
                165                 170                 175

Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
            180                 185                 190

Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
        195                 200                 205

Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
    210                 215                 220

His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His
225                 230                 235                 240

Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
                245                 250                 255

Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
            260                 265                 270

Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
        275                 280                 285

Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
    290                 295                 300

Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
305                 310                 315                 320

Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
                325                 330                 335


<210> 15
<211> 343
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 191-527,
      modified

<400> 15
Ser Glu Gly Asn Ser Asp Thr His Ser Leu Thr Glu Ser Gly Ala Ser
  1               5                  10                  15

Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala
             20                  25                  30

Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys
         35                  40                  45

Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn
     50                  55                  60

Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys
 65                  70                  75                  80

Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu
                 85                  90                  95

Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys
```

```
            100                 105                 110

His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile
        115                 120                 125

Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe
    130                 135                 140

Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val
145                 150                 155                 160

Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His
                165                 170                 175

Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln
            180                 185                 190

Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg
        195                 200                 205

Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu
    210                 215                 220

Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr
225                 230                 235                 240

Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg
                245                 250                 255

Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu
            260                 265                 270

Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp
        275                 280                 285

Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly
    290                 295                 300

Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln
305                 310                 315                 320

Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp
                325                 330                 335

Ile Arg Asp Asn Met Arg Pro
            340
```

<210> 16
<211> 343
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 191-527, modified

<400> 16

```
Ser Glu Gly Asn Ser Asp Thr His Ser Leu Thr Glu Ser Gly Ala Ser
  1               5                  10                  15

Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala
```

```
                20                  25                  30

Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys
          35                  40                  45

Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn
     50                  55                  60

Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Ser Ser Thr Cys
 65                  70                  75                  80

Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu
                85                  90                  95

Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys
            100                 105                 110

His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile
        115                 120                 125

Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe
    130                 135                 140

Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val
145                 150                 155                 160

Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His
                165                 170                 175

Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln
            180                 185                 190

Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg
        195                 200                 205

Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu
    210                 215                 220

Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr
225                 230                 235                 240

Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg
                245                 250                 255

Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu
            260                 265                 270

Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp
        275                 280                 285

Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly
    290                 295                 300

Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln
305                 310                 315                 320

Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp
                325                 330                 335

Ile Arg Asp Asn Met Arg Pro
            340
```

<210> 17
<211> 308
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 220-527

<400> 17

```
Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro
  1               5                  10                  15

Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu
             20                  25                  30

Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg
         35                  40                  45

Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp
     50                  55                  60

Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg
 65                  70                  75                  80

Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys
                 85                  90                  95

Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His
            100                 105                 110

His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu
        115                 120                 125

Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe
    130                 135                 140

Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser
145                 150                 155                 160

Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys
                165                 170                 175

Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu
            180                 185                 190

Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg
        195                 200                 205

Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser
    210                 215                 220

Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly
225                 230                 235                 240

Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln
                245                 250                 255

Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr
            260                 265                 270

Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val
        275                 280                 285
```

```
Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp
    290                 295                 300

Asn Met Arg Pro
305
```

<210> 18
<211> 268
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: K2S 260-527

<400> 18

```
Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg
  1               5                  10                  15

Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala
             20                  25                  30

Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys
         35                  40                  45

Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys
     50                  55                  60

Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg
 65                  70                  75                  80

Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu
                 85                  90                  95

Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp
            100                 105                 110

Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu
        115                 120                 125

Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu
    130                 135                 140

Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala
145                 150                 155                 160

Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu
                165                 170                 175

Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val
            180                 185                 190

Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln
        195                 200                 205

Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
    210                 215                 220

Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly
225                 230                 235                 240

Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr
```

```
                245                 250                 255

Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
            260                 265
```

<210> 19
<211> 527
<212> PRT
<213> Homo sapiens

<400> 19

```
Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
  1               5                  10                  15

Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
             20                  25                  30

Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
         35                  40                  45

Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
     50                  55                  60

Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
 65                  70                  75                  80

Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln
                 85                  90                  95

Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu
            100                 105                 110

Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly
        115                 120                 125

Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys
    130                 135                 140

Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala
145                 150                 155                 160

Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
                165                 170                 175

Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His
            180                 185                 190

Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
        195                 200                 205

Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
    210                 215                 220

Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
225                 230                 235                 240

Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
                245                 250                 255

Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
            260                 265                 270
```

```
Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
        275                 280                 285

Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
    290                 295                 300

Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
305                 310                 315                 320

Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
                325                 330                 335

Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
            340                 345                 350

Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
        355                 360                 365

Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
    370                 375                 380

Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
385                 390                 395                 400

Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
                405                 410                 415

His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His
            420                 425                 430

Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
        435                 440                 445

Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
    450                 455                 460

Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
465                 470                 475                 480

Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
                485                 490                 495

Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
            500                 505                 510

Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
        515                 520                 525
```

<210> 20
<211> 12
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: coding sequence for SEGN

<400> 20
tctgagggaa ac 12

<210> 21
<211> 22
<212> PRT
<213> Escherichia coli

<400> 21
Met Lys Lys Thr Ala Ile Ala Ile Ala Val Ala Leu Ala Gly Phe Ala
1 5 10 15

Thr Val Ala Gln Ala Ala
20

<210> 22
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 22
gaggaggagg tggcccaggc ggcctctgag ggaaacagtg ac 42

<210> 23
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 23
gaggaggagc tggccggcct ggcccggtcg catgttgtca cg 42

<210> 24
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 24
acatgcgacc gtgacaggcc ggccag 26

<210> 25
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 25
ctggccggcc tgtcacggtc gcatgt 26